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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/031,639

05/09/2002

Luigi Naldini

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6785

22462

7590

03/28/2006

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EXAMINER

GUZO, DAVID

ART UNIT

PAPER NUMBER

1636

DATE MAILED: 03/28/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

10/031,639

Applicant(s)

NALDINI ET AL.

Examiner

David Guzo

Art Unit

1636

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 04 January 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 8-10 and 13-32 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 26-28 is/are allowed.
- 6) ☒ Claim(s) 8-10, 13-25 and 29-32 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)             | 4) <input type="checkbox"/> Interview Summary (PTO-413)                     |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)    | Paper No(s)/Mail Date. _____  |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____   | 6) <input type="checkbox"/> Other: _____                                    |

### **Detailed Action**

The sequence listing filed 9/8/05 has been entered.

The indicated allowability of claim 17 is withdrawn in view of the newly discovered reference(s) to Dull et al. in view of Leboulch et al. Rejections based on the newly cited reference(s) follow.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 8-10, 13-25 and 30-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dull et al. in view of Leboulch et al.

Applicants claim a lentiviral (which can be based upon HIV-1) packaging system comprising a structural lentiviral vector system comprising a first lentiviral vector that

encodes a gag gene and a second lentiviral vector encoding a pol gene, and a RRE downstream of the structural (gag or pol) gene and a regulatory lentiviral vector comprising a rev gene (which can be operably linked to a heterologous regulatory element such as RSV U3 or HSV tk promoter) wherein the regulatory lentiviral vector is provided on a separate construct from the structural lentiviral vector and a lentiviral transfer vector comprising a heterologous gene operably linked to a regulatory element. The instant lentiviral packaging system also lacks a functional tat gene (which is mutated to be non-functional or is deleted), comprises a heterologous viral env gene which can be on a separate construct and lacks the lentiviral accessory genes vif, vpr, vpu and nef. Applicants also claim a method of producing a recombinant lentivirus comprising: (a) transfecting a packaging host cell with a lentiviral transfer vector comprising a heterologous gene operably linked to a regulatory element and the instantly claimed lentiviral packaging system and (b) recovering the recombinant lentivirus produced by the transfected packaging host cell.

Dull et al. (Cited by applicants. J. Virol., Nov. 1998, Vol. 72, No. 11, pages 8463-8471 , see whole article, particularly the Abstract, the first eight paragraphs of the "Materials and Methods" section on pages 8464-8465, the first five paragraphs of the "Results" section and Fig. 4) recites a HIV-I based packaging system comprising a structural vector system comprising a first lentiviral vector that encodes gag and pol genes under control of a CMV promoter and a RRE downstream of the gag/pol genes and a regulatory lentiviral vector comprising a rev gene (which can be operably linked to a heterologous regulatory element such as RSV U3 or HSV tk promoter) wherein the

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regulatory lentiviral vector is provided on a separate construct from the structural lentiviral vector and a lentiviral transfer vector comprising a heterologous gene operably linked to a regulatory element. The lentiviral packaging system disclosed by Dull et al. also lacks a functional tat gene (which is mutated to be non-functional), comprises a heterologous viral env gene (VSV-G) which can be on a separate construct and lacks the lentiviral accessory genes vif, vpr, vpu and nef. Dull et al. also recites a method of producing a recombinant lentivirus comprising: (a) transfecting a packaging host cell with a lentiviral transfer vector comprising a heterologous gene operably linked to a regulatory element and the instantly claimed lentiviral packaging system and (b) recovering the recombinant lentivirus produced by the transfected packaging host cell. Dull et al. does not teach separating the gag and pol genes on separate vectors and Dull et al. does not teach deleting the tat gene.

Leboulch et al. (US 6,365,150, issued 4/2/2002, priority to 5/13/1998, see whole document, particularly the Abstract, Figs.1-2 and column 3) recites the desirability of separating the gag and pol genes onto two separate vectors and the desirability of mutating or deleting accessory genes such as tat.

The ordinary skilled artisan, seeking to develop an improved lentiviral vector system would have been motivated to combine the teachings of Dull et al. on the generation of a lentiviral vector system with the gag and pol genes on a single vector with the teachings of Leboulch et al. on separating the gag and pol genes onto two separate vectors and subsequently separate the gag and pol genes onto two separate vectors because Leboulch et al. indicates that separation of the lentiviral structural

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genes onto different vectors reduces the likelihood of recombination with other retroviral sequences within the cell leading to production of unwanted, and potentially dangerous, replication competent helper viruses. It would have been obvious for the ordinary skilled artisan to separate the gag and pol genes onto two different lentiviral vectors because Leboulch et al. teaches that separating the gag and pol genes onto different vectors makes undesirable recombination between the lentiviral sequences and any retroviral sequences present in the packaging cells less likely.

With regard to deletion of the tat gene, Dull et al. teaches that the tat gene was inactivated by mutation (one mutation was deletion of the T in the ATG initiation codon of the tat gene) not by deletion of the gene. However, the mutation of the ATG initiation codon taught by Dull et al. is equivalent to deletion of the gene because no gag protein will be produced in either case. If the purpose of the invention is to generate a lentiviral vector system which does not express tat, Dull et al. and the instant claims accomplish the same thing and absent evidence to the contrary, must be considered to be equivalent. Nevertheless, Leboulch et al. also recites mutation or **deletion** of lentiviral accessory genes such as tat in the generation of a lentiviral vector system with the purpose being to remove said accessory genes from the vector system. The ordinary skilled artisan would therefore have been motivated to remove the tat gene by deletion because Leboulch et al. teaches that deletion of the tat gene reduces the lentiviral sequences present in the cell and hence reduces the likelihood of recombination between the different vectors and between any retroviral sequences present in the cells which could result in generation of undesirable replication competent virus. It would

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have been obvious to remove the tat gene by deletion because Leboulch et al. teaches that minimizing the lentiviral sequence present in the vector system is desirable in order to avoid undesirable homologous recombination which could lead to generation of replication competent lentivirus.

Given the teachings of the prior art and the level of skill of the ordinary skilled artisan at the time the instant invention was made, it must be considered that said ordinary skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 29 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 29 is vague because there is no antecedent basis for the term "the 3' HIV U3 region" in the claims from which claim 29 depends.

Given the withdrawal of the previously made rejections and the new grounds of rejection applied in this Office Action, applicants' arguments filed 3/14/05 are moot.

Any rejections not repeated in this Office Action are withdrawn.

Claims 26-28 are allowed.


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Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Guzo, Ph.D., whose telephone number is (571) 272-0767. The examiner can normally be reached on Monday-Thursday from 8:00 AM to 5:30 PM. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel, Ph.D., can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

David Guzo  
March 15, 2006

  
DAVID GUZO  
PRIMARY EXAMINER